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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,122	12/23/2005	Makoto Ono	282359US0PCT	5544
22850	7590	10/27/2008		
OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314				
EXAMINER				
LOEWY, SUN JAE Y				
ART UNIT		PAPER NUMBER		
1626				
NOTIFICATION DATE		DELIVERY MODE		
10/27/2008		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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### Office Action Summary

**Application No.**

10/562,122

**Applicant(s)**

ONO ET AL

**Examiner**

SUN JAE Y. LOEWE

**Art Unit**

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-7 and 16-19 is/are pending in the application.
- 4a) Of the above claim(s) 5,6 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 7 and 16-18 is/are rejected.
- 7) ☒ Claim(s) 1-4 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

1. Claims 1-7 and 16-19 are pending in the instant application. Claims 5, 6 and 19 withdrawn.

***Response to Amendment***

2. The amendments to the claims filed on August 14, 2008 have been fully considered. The 35 USC 112 1<sup>st</sup> paragraph rejection has been overcome and is thus hereby withdrawn.

3. Prosecution is still limited to the elected species (see Section 2, office action dated May 1, 2008), as the generic claims encompassing the species are not allowable – see new ground of rejection set forth herein, Section 6.

***Claim Objections***

4. Claims 1-3, 7, 16 and 17 objected to for containing non-elected subject matter. Applicant will be entitled to rejoinder of non-elected species upon allowability of the generic claims.

5. Claim 4 objected for being dependent on a base objected claim but would be allowable if re-written in independent form.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 7 and 16-18 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states “There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue”. The factors are applied below to the instant claims.

*The breadth of the claims and nature of invention*

Medicines comprising the elected polymorphic form of

Sodium trans-4-[1-[2,5-dichloro-4-[(1-methyl-1H-3-

indolylcarbonyl)amino]phenylacetyl]-(4S)-methoxy(2S)-

pyrrolidinylmethoxy]cyclohexanecarboxylate pentahydrate.

, which broadly encompasses pharmaceutical compositions (eg. including aqueous).

*The state of the prior art and level of predictability*

It is well known that polymorphs convert to thermodynamically preferred forms unintentionally upon exposure to the energetics of pharmaceutical processing (Brittain et al., p. 332 1<sup>st</sup> paragraph, p. 334 1<sup>st</sup> paragraph), for example: production of bulk drug substance (Brittain et al., p. 333), particle size reduction (Brittain et al., p. 334), granulation (Brittain et al., p. 339). Furthermore, it is known in the art that the solid structure of a compound is lost when that compound is placed in solution (for example, see 1<sup>st</sup> paragraph 1, page 2 of Express-Pharma-Online). Therefore, the level of predictability is low in the art for preserving a particular crystalline form through the process of making a pharmaceutical composition. Absent a teaching of how the instantly

claimed crystalline form can be maintained through the steps involved in pharmaceutical processing, one of ordinary skill would not know how to prepare pharmaceutical compositions of the instantly claimed crystalline form, while avoiding potential transformations that likely occur during the formulation process.

*The amount of direction and working examples provided*

No working examples of the claimed pharmaceutical compositions are provided. No guidance is given for the method of making pharmaceutical compositions while maintaining the specifically claimed crystal form.

*The quantity of experimentation needed to make or use the invention*

Based on the lack of direction in the instant disclosure, in view of the low level of predictability in the art, one of ordinary skill is not enabled to make pharmaceutical compositions of any claimed polymorphic form. The quantity of experimentation to practice the claimed invention is undue.

***Conclusion***

7. No claims allowed.
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUN JAE Y. LOEWE whose telephone number is (571)272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sun Jae Y. Loewe, Ph.D./  
10-17-2008

/Kamal A Saeed, Ph.D./  
Primary Examiner, Art Unit 1626